

## APPENDIX A

### Version to Show Changes Made

1. A chimeric peptide comprising a  $\mu$  [an N-terminal] opioid receptor binding moiety at its N-terminus and [a C-terminal] an agonist Substance P receptor [agonist] binding moiety at its C-terminus, wherein said peptide induces analgesia.
28. The peptide of claim [27] 1, wherein said opioid receptor binding moiety is a  $\mu$  receptor agonist.
31. The peptide of claim 30 wherein said opioid receptor binding moiety is [selected from the group consisting of peptides] a peptide having any one of SEQ ID Nos: 1-11, or an N-terminal [fragments and] fragment or N-terminal [derivatives] derivative thereof.
32. The peptide of claim 30 wherein said opioid receptor binding moiety is endomorphin 1, endomorphin 2, an N-terminal [fragment] fragment, or an N-terminal derivative thereof.
33. The peptide of claim 32 wherein said opioid receptor binding moiety is [selected from the group consisting of peptides] a peptide having [SEQ ID Nos: 2-3] SEQ ID No: 2 or 3, or an N-terminal [fragments and] fragment or N-terminal [derivatives] derivative thereof.
45. The peptide of claim 1, [24 or 25] wherein said agonist Substance P receptor [agonist] binding moiety comprises Substance P, a C-terminal Substance P [fragment] fragment, or a C-terminal Substance P derivative.
46. The peptide of claim 1, [24 or 25] wherein the  $-\text{COOH}$  moiety of the C-terminal amino acid residue of said Substance P receptor binding moiety is protected.

49. The peptide of claim 48 wherein said Substance P receptor binding moiety is [selected from the group consisting of peptides] a peptide having any one of SEQ ID Nos: 21, 36 and 38-41, or a C-terminal [N-terminal fragments and] fragment or C-terminal [N-terminal derivatives] derivative thereof.
53. The peptide of claim 52 wherein said Substance P receptor binding moiety is [selected from the group consisting of peptides] a peptide having any one of SEQ ID Nos: 25-27, or a C-terminal [N-terminal fragments and] fragment or C-terminal [N-terminal derivatives] derivative thereof.
56. The peptide of claim 55 wherein said Substance P receptor binding moiety is [selected from the group consisting of peptides] a peptide having any one of SEQ ID Nos: 28-30, or a C-terminal [N-terminal fragments and] fragment or C-terminal [N-terminal derivatives] derivative thereof.
57. The peptide of claim 1 wherein the opioid receptor binding moiety is [selected from the group consisting of] endomorphin 1, endomorphin 2, or an N-terminal [fragments and] fragment or N-terminal [derivatives] derivative thereof; and the Substance P receptor binding moiety is [selected from the group consisting of] Substance P, or a C-terminal [fragments and] fragment or C-terminal [derivatives] derivative thereof.
61. The peptide of claim [60] 1 wherein said peptide comprises at least one D-amino acid.
64. The pharmaceutical composition of claim 62, wherein said peptide induces analgesia when administered to a mammal.
69. The pharmaceutical composition of claim [68] 62, wherein said opioid receptor binding moiety is a  $\mu$  receptor agonist.

70. The pharmaceutical composition of claim 69 wherein the N-terminal amino acid residue of said opioid receptor binding moiety is a free amine.
71. The pharmaceutical composition of claim 70 wherein the N-terminal amino acid residue of said opioid receptor binding moiety is Tyr.
72. The pharmaceutical composition of claim 71 wherein said opioid receptor binding moiety is [selected from the group consisting of peptides] a peptide having any one of SEQ ID Nos: 1-11, or an N-terminal [fragments and] fragment or N-terminal [derivatives] derivative thereof.
73. The pharmaceutical composition of claim 71 wherein said opioid receptor binding moiety is endomorphin 1, endomorphin 2, an N-terminal [fragment] fragment, or an N-terminal derivative thereof.
74. The pharmaceutical composition of claim 73 wherein said opioid receptor binding moiety is [selected from the group consisting of peptides] a peptide having [SEQ ID Nos: 2-3] SEQ ID No: 2 or 3, or an N-terminal [fragments and] fragment or N-terminal [derivatives] derivative thereof.
86. The pharmaceutical composition of claim 62, [65 or 66] wherein said agonist Substance P receptor [agonist] binding moiety comprises Substance P, a C-terminal Substance P [fragment] fragment, or a C-terminal Substance P derivative.
87. The pharmaceutical composition of claim 62, [65 or 66] wherein the -COOH moiety of the C-terminal amino acid residue of said Substance P receptor binding moiety is protected.

88. The pharmaceutical composition of claim 87 wherein the -COOH moiety of the C-terminal amino acid residue of said Substance P receptor binding moiety is amidated.
89. The pharmaceutical composition of claim 88 wherein the C-terminal amino acid residue of said Substance P receptor binding moiety is Met-NH<sub>2</sub>.
90. The pharmaceutical composition of claim 89 wherein said Substance P receptor binding moiety is [selected from the group consisting of peptides] a peptide having any one of SEQ ID Nos: 21, 36 and 38-41, or a C-terminal [N-terminal fragments and] fragment or C-terminal [N-terminal derivatives] derivative thereof.
91. The pharmaceutical composition of claim 87 wherein the -COOH moiety of the C-terminal amino acid residue of said Substance P receptor binding moiety is esterified.
92. The pharmaceutical composition of claim 91 wherein the C-terminal amino acid residue of said Substance P receptor binding moiety is a methyl ester.
93. The pharmaceutical composition of claim 92 wherein the C-terminal amino acid residue of said Substance P receptor binding moiety is Gly-OMe, Lys-COOMe or Arg-COOMe.
94. The pharmaceutical composition of claim 93 wherein said Substance P receptor binding moiety is [selected from the group consisting of peptides] a peptide having any one of SEQ ID Nos: 25-27, or a C-terminal [N-terminal fragments and] fragment or C-terminal [N-terminal derivatives] derivative thereof.
95. The pharmaceutical composition of claim 91 wherein the C-terminal amino acid residue of said Substance P receptor binding moiety is an ethyl ester.

96. The pharmaceutical composition of claim 95 wherein the C-terminal amino acid residue of said Substance P receptor binding moiety is Gly-COOEt, Lys-COOEt or Arg-COOEt.
97. The pharmaceutical composition of claim 96 wherein said Substance P receptor binding moiety is [selected from the group consisting of peptides] a peptide having any one of SEQ ID Nos: 28-30, or a C-terminal [N-terminal fragments and] fragment or C-terminal [N-terminal derivatives] derivative thereof.
98. The pharmaceutical composition of claim 62 wherein the opioid receptor binding moiety is [selected from the group consisting of] endomorphin 1, endomorphin 2, or an N-terminal [fragments and] fragment or N-terminal [derivatives] derivative thereof; and the Substance P receptor binding moiety is [selected from the group consisting of] Substance P, or a C-terminal [fragments and] fragment or C-terminal [derivatives] derivative thereof.
99. The pharmaceutical composition of claim 62 wherein the peptide has SEQ ID No: 42.
100. The pharmaceutical composition of claim 62 wherein the peptide has SEQ ID No: 43.
102. The pharmaceutical composition of claim [101] 62 wherein said peptide comprises at least one D-amino acid.